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EXAMINER	
ALSTRUM ACEVEDO, JAMES HENRY	
ART UNIT	**PAPER NUMBER**
1616	

DATE MAILED: 12/01/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/663,010	CLAROT ET AL.	
	Examiner	Art Unit	
	James H. Alstrum-Acevedo	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☒ Claim(s) *1 and 11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *June 4, 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-31 are pending.

Specification

The disclosure is objected to because of the following informalities: two typographical errors were observed in paragraphs [0030] and [0033] on lines 9 and 5, respectively. These typographical errors are: (1) misspelling of the word "active" as "ative" on line 9 of [0030] and (2) misspelling the word "thickeners" on line 5 of [0033] as "thickness."

Appropriate correction is required.

Claims 1 and 11 are objected to because of the following informalities: the claim language following the colon on lines 5 and 4, respectively is confusing with regards to which species are intended as viable thickeners and which are intended as other acceptable adjuvants/excipients. The Examiner respectfully suggests using the following language "...wherein said thickener is selected from the group consisting of carrageenan, sugar, guar gum, methylcellulose, carbohydrate thickeners, aloe vera, and the like (see [0016] in the specification). The composition further comprises a about 0.001 to about 5.0 weight percent of a decongestant, and optionally further comprises antiseptics, preservatives, permeation enhancers, sequestering agents, buffers, and emulsifiers, wherein the composition has a viscosity greater than about 2,500 centipoise. Appropriate correction is required.

Claim 12 is objected to because of the following informalities: the word "homeopathic" on line 5 of said claim is misspelled as "homoepathic". Appropriate correction is required.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 12 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for decongestants, does not reasonably provide enablement for vitamins, minerals, nucleic acids, amino acids, peptides, polypeptides, proteins, genes, mutagens, antiviral agents, antibacterial agents, anti-inflammatory agents, histamines, anti-histamines, anti-allergens, allergy-relief substances, homeopathic substances, and pharmaceutical substances. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. Analysis of claim 12 per the Wands factors follows.

(A) Breadth of the Claim

Claim 12 is extremely broad as it is drawn to compositions intended for the delivery of at least one active substance to the nasal membrane (i.e. this implies these are pharmaceutical compositions intended for some kind of treatment) in which the active agent may be vitamins, minerals, nucleic acids, amino acids, peptides, polypeptides, proteins, genes, mutagens, antiviral agents, antibacterial agents, anti-inflammatory agents, decongestants, histamines, anti-histamines, anti-allergens, allergy-relief substances, homeopathic substances, and pharmaceutical substances. The possible active agent(s) encompasses a seemingly infinite number of compounds.

(B) The Nature of the Invention

Upon reading the claims and specification of the instant application, the Examiner concludes that the nature of the instant invention focuses on (1) pharmaceutical formulations comprising decongestants as the active agent, which improve the adherence of said formulations to the nasal membrane and (2) methods of delivering said pharmaceutical formulations. The nature of the invention does not encompass formulations or delivery methods that do not contain decongestants. The possibility that the active agents may be other than decongestants is mentioned only in passing on pages 19 and 20 of the specification, [0054-0055].

(C) State of the Prior Art /Level of Predictability

As an illustrative example, the Examiner makes reference to the state of the prior art regarding the stability of proteins and what information is required for a person of ordinary skill in the art to use proteins as active agents. It is well known in the art that proteins may be denatured (i.e. lose their biological activity) due to mild changes in physical conditions including changes in pH, temperature (both heating and cooling), and exposure to aqueous solutions of organic compounds (e.g. detergents (i.e. surfactants), ethanol, urea, guanidine) (Smith et al. *Principles of Biochemistry: General Aspects*, McGraw-Hill: New York, 1983, pp 29 and 56-57). It is also art-recognized that proteins are the most functionally diverse of all biological compounds and that it is difficult to predict the reasons why a protein is denatured at certain pH values, whereas other proteins are not (ibid, pp 23 and 27). This demonstrates that there is a high level of unpredictability in the art.

(D) Level of One of Ordinary Skill in the Art

The level of a person of ordinary skill in the art is high with artisans typically having an advanced degree (Ph.D., M.D., Pharm. D., or combination thereof).

(E) Amount of Direction Provided by the Inventor

The inventor only provides direction regarding formulations comprising decongestants. The inventor provides no direction regarding formulations comprising one or more of the following active agents: vitamins, minerals, nucleic acids, amino acids, peptides, polypeptides, proteins, genes, mutagens, antiviral agents, antibacterial agents, anti-inflammatory agents, histamines, anti-histamines, anti-allergens, allergy-relief substances, homeopathic substances, and pharmaceutical substances.

(F) The Existence of Working Examples

The only working examples provided are for formulations comprising known decongestants (i.e. oxymetazoline HCl). See Examples 1 and 2. No working examples are provided regarding formulations comprising non-decongestant active agents.

(G) Quantity of Experimentation Needed to Make/Use the Invention

The person of ordinary skill in the art would require an undue quantity of experimentation in order to modify the formulations of the instant application, so that they could be used with any active agent belonging to the following group: vitamins, minerals, nucleic acids, amino acids, peptides, polypeptides, proteins, genes, mutagens, antiviral agents, antibacterial agents, anti-inflammatory agents, histamines, anti-histamines, anti-allergens, allergy-relief substances, homeopathic substances, and pharmaceutical substances.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 12 uses the terms "homeopathic substances" however, neither the claim nor the specification define what constitutes a homeopathic substance. A person of ordinary skill in the art would not be able to ascertain what compounds or ingredients Applicant intends to encompass with the term "homeopathic substance." Likewise the term "pharmaceutical substances" is indefinite, because the word substance is defined in the specification on page 20 as being equivalent to "ingredient." The term "pharmaceutical ingredient" encompasses both pharmaceutically acceptable excipients as well as active agents; therefore the Examiner respectfully requests clarification.

Claim 12 is confusing because it utilizes the term "allergy-relief substances" as well as anti-histamines, which are used to treat allergies. It is unclear what is the difference between "allergy-relief substances" and anti-histamines.

The term "allergy-relief substances" is not defined in the specification. It is unclear if the Applicant intends this term to solely encompass anti-histamines or whether it includes other substances. If the Applicant's intention is the latter, it is unclear what the other substances may be. Clarification is requested.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1, 2, 11-15, and 27-29 are rejected under 35 U.S.C. 102(a) as being anticipated by Davidson et al. (U.S. Patent No. 6,365,624).

Davidson teaches a composition for reducing the duration of a common cold comprising: about **90 to about 99.1 weight percent of a carrier**; **about 0.9 to about 2.0 weight percent zinc gluconate**, wherein said composition has a **viscosity greater than about 5,000 centipoise**, wherein the carrier includes **glycerin** in an amount of about **0.05 to about 3.0 weight percent,** further comprising a thickener selected from the group consisting of: **carbohydrate thickeners, carrageenan, sugar, guar gum, and methylcellulose**, and further comprising about **0.01 to about 0.10 weight percent methanol** (claims 9-14).

Davidson also teaches **a method of applying a zinc gel composition to a nasal membrane** (claims 1-8).

Davidson teaches that ionic zinc is a known effective anti-rhinovirus agent in vitro and in vivo (column 1, lines 21-22).

Davidson teaches that **zinc in the nasal cavity acts as a decongestant**, enhancing the discharge of mucous and inhibiting the generation of new mucous. **Menthol is also a decongestant** and a bronchial dilator (column 6, lines 1-8).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 3-10 and 16-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davidson (U.S. Patent No. 6,365,624) as applied to claims 1, 2, 11-15, and 27-29 above, and further in view of Haslwanter et al. (U.S. Patent No. 5,854,269).

The teachings of Davidson have been set forth above.

Davidson lacks the teaching of decongestant compositions comprising permeation enhancers, preservatives, emulsifiers, and buffers.

Haslwanter teaches that an over-the-counter (OTC) product under the trade name AFRIN® comprises a composition containing vapors of **menthol**, **eucalyptol** and **camphor, oxymetazoline hydrochloride,** and an aqueous carrier containing **benzalkonium chloride**, **glycerine**, phenylmercuric acetate, sorbitol, polysorbate 80 is currently available (column 1, lines 37-44).

Haslwanter teaches in nasal compositions comprising **oxymetazoline or a pharmaceutically acceptable salt thereof** in the range of about **0.01 % to about 0.1 % by weight/volume (w/v)**, **benzyl alcohol (a preservative)** in an amount from about **0.10 to 5.00 % w/v**, a surfactant (i.e. emulsifier) from about 0 to 2.00 % w/v, **disodium EDTA** from about 0 to 0.1 % w/v, **benzalkonium chloride** from about 0.01 % to 0.3 % w/v, and pharmaceutically acceptable **buffers**, including **phosphate**. In Example 2, Haslwanter teaches several specific surfactants, including a **fatty acid ester of polyethylene glycol, and specific buffers (sodium phosphate monobasic and sodium phosphate dibasic)** (i.e. Polysorbate 80) (column 2, lines 40-45, 56-60, 65-67; column 3, lines 1, 13-15, 23-27, 28-33; and Example 2). Examples 3-5 teach similar compositions too.

It would have been obvious to a person of ordinary skill in the art at the time of the instant invention to combine the teachings of Davidson and Haslwanter, because it is obvious to combine known decongestants per the teaching of Davidson and a commercially available OTC decongestant at the time of the instant invention was known to comprise a mixture of decongestants, water, an emulsifier, and a preservative. Haslwanter does not teach disodium EDTA as a permeation enhancer, nonetheless this is a property of disodium EDTA, and a compound cannot be separated from its properties. As a result, Haslwanter's compositions

obviously contained a permeation enhancer. A skilled artisan would have had a reasonable expectation of success upon combining the teachings of Davidson and Haslwanter, because both teach aqueous decongestant compositions comprising menthol and glycerine had been used in the art at the time of the instant invention in an OTC decongestant containing components similar to the teachings of Haslwanter. Regarding the amounts of components state in the instant application, the amount of a specific ingredient in a composition is clearly a result effective parameter that a person of ordinary skill in the art would routinely optimize. Optimization of parameters is a routine practice that would be obvious for a person of ordinary skill in the art to employ. It would have been customary for an artisan of ordinary skill to determine the optimal amount of each ingredient needed to achieve the desired results. Thus, absent some demonstration of unexpected results from the claimed parameters, the optimization of ingredient amounts would have been obvious at the time of applicant's invention.

Claims 30-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Davidson (U.S. Patent No. 6,365,624) in view of Haslwanter et al. (U.S. Patent No. 5,854,269) as applied to claims 3-10 and 16-16 above, and further in view of Pier (U.S. Patent No. 6,245,735).

The teachings of Davidson and Haslwanter have been set forth above.

Davidson lacks the teaching of liposomes.

Pier teaches pharmaceutical compositions for gene therapy, treating *P. aeruginosa* infection, and upregulating cystic fibrosis transmembrane conductance regulators (abstract).

Pier teaches covalently conjugated polysaccharide **liposomes** containing virtually any bioactive agent within the liposome, including **nasal decongestants** (column 3, lines 30-38 and column 9, lines 15-18 and 65).

Pier teaches that the manufacture of liposomes containing bioactive agents is fully described in the literature (column 8, lines 47-49).

It would have been obvious to a person or ordinary skill in the art at the time of the instant invention to combine the teachings of Davidson and Haslwanter with the teachings of Pier, because the manufacture of liposomes containing bioactive agents (e.g. nasal decongestants) is fully described in the literature. Therefor, it would have been apparent to a skilled artisan to include liposomes as part of a nasal decongestant formulation and this would have also provided the motivation to use liposomes. A person of ordinary skill in the art at the time of the instant invention would have had a reasonable expectation of successfully incorporating liposomes as permeation enhancers, because liposomes are well known in the art, per the teachings of Pier.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned

with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claim 29 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of copending Application No. 10/664,839 (copending '839). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims are overlapping in scope.

The combined limitations of claim 1-11 of copending '839 are obvious over the limitations of claim 29 of the instant application, including an active substance (e.g. decongestant, such as oxymetazoline hydrochloride), glycerin, carrageenan, sugar, guar gum, methylcellulose, carbohydrate thickeners, aloe, permeation enhancers, preservatives, and sequestering agents.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claims 1 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 23-29 and 34 of copending Application No. 11/028,991 (copending '991). Although the conflicting claims are not identical, they are not patentably distinct from each other because these claims are overlapping in scope.

The combined limitations of claim 23-29 and 34 of copending '991 are obvious over the limitations of claims 1 and 11 of the instant application, including an active substance (e.g. decongestant, such as oxymetazoline hydrochloride), glycerin, carrageenan, sugar, guar gum, methylcellulose, carbohydrate thickeners, and permeation enhancers.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Conclusion

The specification and claims 1 and 11 are objected. Claims 1-31 are rejected. No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James H. Alstrum-Acevedo whose telephone number is (571) 272-5548. The examiner can normally be reached on M-F, 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (571) 272-0887. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James H. Alstrum-Acevedo, Ph.D.
Examiner

SREENI PADMANABHAN
SUPERVISORY PATENT EXAMINER